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Resorbable, well tolerated bone implant material obtained from powdered hydroxylapatite nanoparticles and calcium sulfate, useful e.g. for filling bone defects or as a drug carrier

Patent Assignee: CORIPHARM MEDIZINPRODUKTE GMBH & CO KG (CORI-N)

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8 patents, 20 countries

#### Patent Family

Patent Number	Kind	Date	Application Number	Kind	Date	Update
WO 2001034216	A1	20010517	WO 2000EP10133	A	20001014	200138 B
DE 19953771	C1	20010613	DE 19953771	A	19991109	200138 E
EP 1227851	A1	20020807	EP 2000975867	A	20001014	200259 E
			WO 2000EP10133	A	20001014	
JP 2003513711	W	20030415	WO 2000EP10133	A	20001014	200328 E
			JP 2001536211	A	20001014	
EP 1227851	B1	20030507	EP 2000975867	A	20001014	200333 E
			WO 2000EP10133	A	20001014	
DE 50002122	G	20030612	DE 50002122	A	20001014	200340 E
			EP 2000975867	A	20001014	
			WO 2000EP10133	A	20001014	
US 6689375	B1	20040210	WO 2000EP10133	A	20001014	200413 E
			US 2002129753	A	20020605	
ES 2199185	T3	20040216	EP 2000975867	A	20001014	200416 E

Priority Applications (no., kind, date): DE 19953771 A 19991109

#### Patent Details

Number	Kind	Lan	Pg	Dwg	Filing Notes
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WO 2001034216	A1	DE	25	0	
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National Designated States,Original: JP US

Regional Designated States,Original: AT BE CH CY DE DK ES FI FR GB GR IE  
IT LU MC NL PT SE

EP 1227851	A1	DE			
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PCT Application WO 2000EP10133

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Regional Designated States,Original: AT BE CH CY DE DK ES FI FR GB GR IE  
IT LI LU MC NL PT SE

JP 2003513711	W	JA	19		
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PCT Application WO 2000EP10133

Based on OPI patent WO 2001034216

EP 1227851	B1	DE			
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PCT Application WO 2000EP10133

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Regional Designated States,Original: DE ES FR GB IT

DE 50002122	G	DE			
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Application EP 2000975867

PCT Application WO 2000EP10133

Based on OPI patent EP 1227851

Based on OPI patent WO 2001034216

US 6689375	B1	EN			
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PCT Application WO 2000EP10133

Based on OPI patent WO 2001034216

ES 2199185	T3	ES			
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Application EP 2000975867

Based on OPI patent EP 1227851

**Alerting Abstract WO A1**

**NOVELTY** - A resorbable bone implant material (I), obtained from powdered components including hydroxylapatite (HAP) and a liquid, where:

- 1.the powder components consist of a mixture of HAP and calcium sulfate (CAS); and
- 2.the HAP powder consists of highly pure, synthetically prepared, crystalline nanoparticles having a crystal width of 10-20 nm and length of 50-60 nm.

**DESCRIPTION** - An INDEPENDENT CLAIM is included for the preparation of (I), by:

- 1.forming a mixture of 85-55 wt. % HAP (as defined above) and 15-45 wt. % CAS powder consisting of highly pure, synthetically prepared alpha-subhydrate (bassanite; having  $nH_2O$ , where n is less than 1, specifically approximately 0.5);
- 2.forming a viscous mass containing the powder mixture and 100-200 wt. % sterile water; and
- 3.forming the mixture into a solid structure.

**USE** - (I) is useful as a bone substitute material, specifically in the fields of orthopedics, traumatology, cranial, jaw or eye surgery or odontology, e.g. for bridging large bone defects after major fractures, fixing small bone chips, filling bone defects (due to osteoclasia, removal of bone tumors, chronic osteomyelitis, loss of alveolar or jaw bone material) and/or as a carrier for drugs (such as antibiotics (claimed), cytostatic agents, growth factors (claimed) or osteogenic agents).

**ADVANTAGE** - The combination of HAP and CAS avoids the disadvantages of either component used alone, e.g. the brittleness of HAP and the excessively rapid degradation of CAS. (I) is a well tolerated, resorbable bone substitute material formed from readily available components of non-biological origin, free of risks of transfer of infections such as hepatitis, HIV or Creutzfeld-Jacob disease. (I) can be prepared with high purity, reproducibility, standardizability and physical/chemical stability, with controllable properties (e.g. water uptake capacity). It is suitable for a wide range of applications (e.g. in 'press-fit' implantation) and forms a clear X-ray image after implantation.

**Technology Focus**

**CERAMICS AND GLASS** - Preferred Materials: The HAP nanocrystals have a specific absorbing BET surface of 100-150 m<sup>2</sup>/g. The CAS powder consists of highly pure, synthetically prepared alpha-subhydrate (bassanite), preferably having a specific absorbing BET surface of 1.8-2.7 (especially 2.0-2.3) m<sup>2</sup>/g and preferably containing 2-15 (especially 5-10) wt. % calcium oxide. The powder mixture contains HAP and CAS particles in a BET surface ratio of ca. 150 : 2; and contains 85-55 (preferably 80-70) wt. % HAP powder.

**Preferred Production:** The particles are sterilized by beta- or gamma-radiation before processing. The viscous mass has a weakly alkaline pH of 7.5-8.2 and a flowable plastic consistency; and is converted into granules (e.g. by molding followed by comminution) or into shaped articles (specifically by molding), preferably spheres, cylinders, prisms or parallelepipeds. (I) is adjusted to a standardized, reproducible water

absorption capacity. After hardening (I) is sterilized with beta- or gamma-radiation or ethylene oxide then packaged under sterile conditions. Before use (I) may be impregnated with one or more sterile solution(s) of pharmaceutically active agents, specifically antibiotics or growth factors.

#### Original Publication Data by Authority

##### Original Abstracts:

Die pulverformige Komponente des Implantatmaterials besteht im wesentlichen aus einer Mischung von Hydroxylapatit- und Kalziumsulfatpulver, wobei das Hydroxylapatitpulver aus synthetisch hergestellten, gefallten hochreinen kristallinen Nano-Partikeln besteht, die eine Kristallgrosse von 10-20 nm Breite und 50-60 nm aufweisen. Die spezifische absorbierende BET-Oberfläche der Nano-Kristalle beträgt dabei vorzugsweise 100-150 m<sup>2</sup>/g.

The invention relates to absorbable bone implant material produced from a powder component containing hydroxylapatite; and a liquid. Said powder component of the implant material essentially consists of a mixture of hydroxylapatite powder and calcium sulphate powder. The hydroxylapatite powder consists of synthetically produced, precipitated, highly pure crystalline nano-particles with a crystal size of 10-20 nm in width and 50-60 nm in length. The specific absorbent BET surface area of the nano-crystals is preferably 100-150m<sup>2</sup>/g.

The powdery component of the implant material consists essentially of a mixture of hydroxyl apatite powder and calcium sulfate powder, wherein the hydroxyl apatite powder consists of synthetically prepared, precipitated crystalline nanoparticles of high purity, which have a crystal size of 10-20 nm width and 50-60 nm length. The specific absorbing BET surface area of the nanocrystals is preferably 100-150 m<sup>2</sup>/g.

Aus einer Hydroxylapatit enthaltenden pulverformigen Komponente und Flüssigkeit aufbereitetes resorbierbares Knochen-Implantatmaterial. Die pulverformige Komponente des Implantatmaterials besteht im wesentlichen aus einer Mischung von Hydroxylapatit- und Kalziumsulfatpulver, wobei das Hydroxylapatitpulver aus synthetisch hergestellten, gefallten hochreinen kristallinen Nano-Partikeln besteht, die eine Kristallgrosse von 10-20 nm Breite und 50-60 nm Länge aufweisen. Die spezifische absorbierende BET-Oberfläche der Nano-Kristalle beträgt dabei vorzugsweise 100-150m<sup>2</sup>/g.

The invention relates to absorbable bone implant material produced from a powder component containing hydroxylapatite; and a liquid. Said powder component of the implant material essentially consists of a mixture of hydroxylapatite powder and calcium sulphate powder. The hydroxylapatite powder consists of synthetically produced, precipitated, highly pure crystalline nano-particles with a crystal size of 10-20 nm in width and 50-60 nm in length. The specific absorbent BET surface area of the nano-crystals is preferably 100-150m<sup>2</sup>/g.